



## Hereditary Multiple Exostoses: A Rare Case Report

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### Abstract

*Hereditary Multiple Exostoses (HME) is a genetically transmitted bone dysplasia that is inherited in an autosomal dominant manner. It usually presents after the age of two years as multiple bony growths on the appendicular skeleton. As a rare condition (incidence of 0.9-2/100,000), it is not commonly seen in our environment. This paper presents the clinical and radiological features of one patient seen in our hospital. Patient who manifested features of hereditary multiple exostoses at the age of fourteen years is presented. The main presenting features were painless progressively increasing bony swellings in both upper and lower limbs. One of them had pressure symptoms which necessitated surgical excision of the symptomatic exostosis. Fine needle aspiration cytology confirmed the diagnosis of osteochondroma. Hereditary multiple exostoses though rare, do occur in our environment and the management is essentially by masterly inactivity except when the bony swellings exhibit any complications or there is concomitant deformity.*

**Keywords:** Hereditary, Multiple, Exostoses, Deformity.

### Introduction

Exostosis is a cartilage capped bony projection found primarily at the juxta-epiphyseal regions of the most rapidly growing ends of long bones<sup>1</sup>. It is the most common bone tumour seen in children<sup>2-4</sup>. The true prevalence is not known since many patients with asymptomatic lesions are never diagnosed. It is considered a hamartoma; as such it stops growing at the end of the growth of the affected bones. In the clinical setting, exostosis presents most commonly as a solitary lesion while

multiple exostoses affecting many bones are much rarely encountered. Patients with HME have multiple cartilage-capped exostoses that may be sessile or pedunculated. Hereditary multiple exostoses is an autosomal dominant skeletal dysplasia affecting bones formed by endochondral ossification. It causes asymmetrical retardation of longitudinal bone growth with subsequent deformity, limb-length inequality and increased risk to secondary malignant transformation.

Limb-length discrepancy is common. A clinically significant inequality of 2cm or greater has been reported with a prevalence ranging from 10-50%<sup>4</sup>. Shortening can occur in the femur and/or the tibia; the femur is affected approximately twice as commonly as the tibia<sup>5</sup>. They have the tendency to cause mechanical interference with the normal function of those soft tissues passing over them. Tendons, muscles, nerves and arteries may all be displaced and irritated by the pressure of the exostosis. The consequence of this is bursitis, hyperaesthesia, pseudo-aneurysm or compression; some or all of which may be the pathogenesis of pain in this condition. The implication of the progressive pathology of the condition is that the clinical presentation may be in three stages. In the first stage, patients will present with multiple lumps at the end of the long bones without any significant pain or deformity. The second stage will feature multiple lumps with pain or deformity while the third stage will consist of multiple lumps, pain and multiple deformities. Management therefore depends on the presentation. In the presence of uncomplicated exostoses, management is essentially by masterly inactivity as these patients have a normal life expectancy.

However, surgical intervention (corrective osteotomy, epiphyseodesis, excision, limb lengthening) is indicated when the exostoses exhibit pressure symptoms, cause deformity or undergo malignant transformation. We hereby present the clinical and radiological features of one patient seen in our hospital with multiple site involvement.

### Case Report

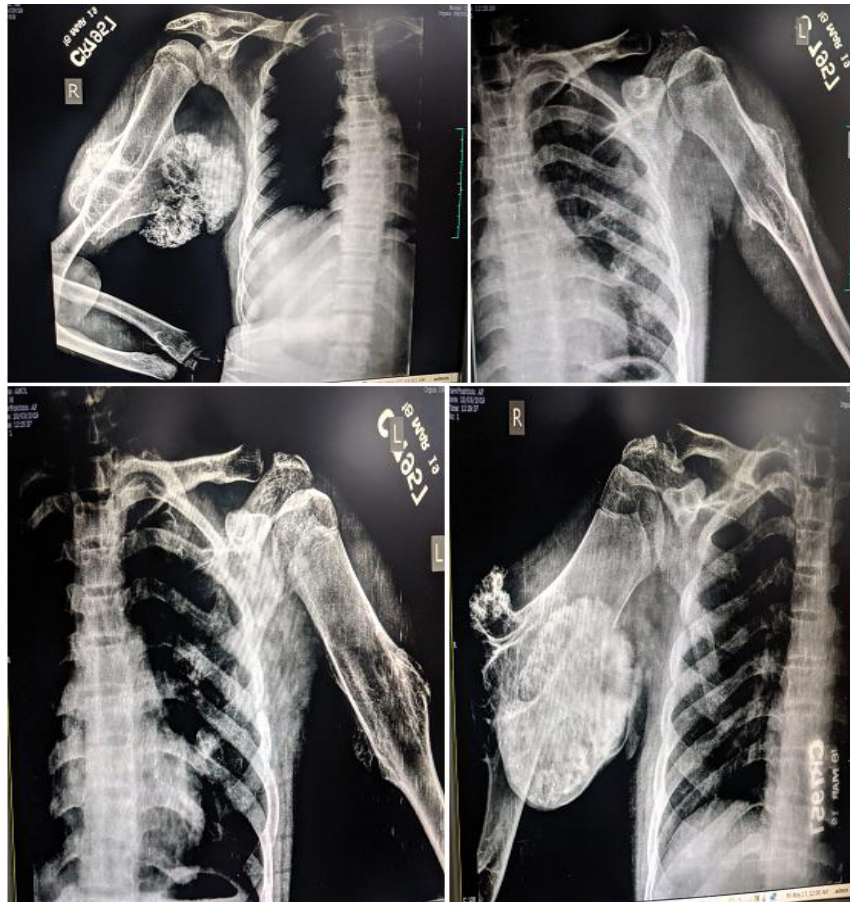
14 year old male who presented at our outpatient clinic with a 7-year history of progressive swellings on both upper limbs and lower limbs. The patient noticed multiple swellings on both shoulders, forearms, and knees. The swellings appeared about the same time. The swellings were initially small in size but they had gradually increased over time. There was no preceding

history of trauma and no fever, cough, weight loss or any other constitutional symptoms. No history of similar swellings in any of his siblings or the parents. There was associated pain especially over the medial aspect of right shoulder and left knee. The pain was described as a constant dull ache which was worse at night. There was no change in the skin colour over the swellings or any ulceration. Essential findings in the musculoskeletal system revealed a tender bony hard swelling on the anteromedial surface of the proximal third of the right arm measuring 10x15cm. There were also non-tender bony hard swellings on the anterolateral surface of the proximal third of the left arm measuring 3x3cm and distal third of the both forearm measuring 2x2cm without ulnar deviation of the wrist. There is associated small swelling at both elbow involving distal humerus and proximal ulna. In the lower limbs, there were also similar bony hard swellings on the medial and lateral surfaces of the distal third of both thighs and the anteromedial surface of the proximal third of both legs. However the swelling on the left distal femur which measures 6x6cm was tender. There was a limb length discrepancy of 2cm with the shortening located in the left leg. There is associated swelling on both proximal femur and distal leg.

There was no neurovascular deficit. The full blood count and the erythrocyte sedimentation rate were within normal limits. X-ray findings in the shoulders revealed bony outgrowths from the proximal ends of both humeri with expansion of the proximal third of the bones and thinning of the cortices. (fig 1a) In the left forearm, there is also expansion of the distal ends of both radius and ulna with left shortening of the ulna (fig 1b). on right side, there is swelling on distal humerus and proximal ulna with proximal R-U subluxation with swelling on distal radius-ulna without any shortening and deformity.(fig 1b) In the knees, there are bony outgrowths in the left distal femoral and proximal tibia metaphyses growing away from the physes. There are mottled opacities

over the top of the outgrowths with expansion of the metaphyseal regions.(fig 2) there is associated swelling in both proximal femur and distal tibia.(fig 2) After x-ray, MRI scan of right proximal humerus and left distal femur was done to see the cartilage cap thickness(On MRI, rt humerus-3 swellings-1 on medial aspect of 7x9 cm with cartilage cap thickness of 3-4mm, 1 on posterior aspect of size 6.2x2.5cm with cap of 3mm and one on lateral aspect of size 3.5x2.8cm with cap thickness of 3mm which look a single large swelling on clinical examination of size 10x15 cm (fig 3), Lt distal femur- larger lesion in medial aspect of 6.9x4.3cm with cap of 2-3mm and lesion on post, aspect of 2.1x1.1cm with cap of 2mm (fig 3). Fine Needle Aspiration and Cytology of the swellings on rt proximal humerus and left distal femur revealed an aspirate consisting of fragments of osteoid, mesenchymal cells and cartilage with numerous plasma cells, lymphoid cells and giant cells. The impression

was that of an exostosis with underlying chronic inflammatory process. A diagnosis of hereditary multiple exostoses with bursitis and or neural compression was made. The patient had excisional biopsy of the painful swellings from the proximal right humerus and left distal femur. Intra-operative findings were right proximal humerus osteochondroma were multiple in number, large, pedunculated and grossly of 7x9cm,6x3cm and 3x3cm and left distal femur were multiple, pedunculated and grossly 7x4 cm, 2x2cm in size. The tumours were shaved off the bone and sent for histopathology which revealed features consistent with exostosis without any malignant change. The postoperative period was uneventful and post-operative x-rays done showed that the excised lesions were no longer visible. The patient has remained pain-free since then. He is still being followed up in the outpatient clinic.



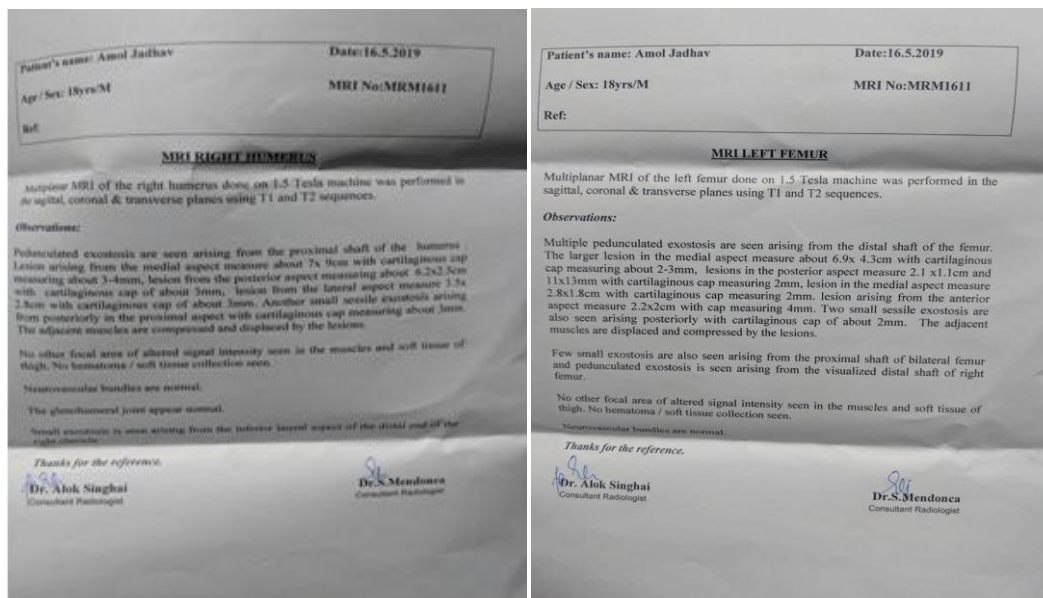
**Fig.1a** bony outgrowths from the proximal ends of both humerus with expansion of the proximal third of the bones and thinning of the cortices.



**Fig.1b** on left side, there is distal radius-ulna bony lesion with ulnar shortening and radial bowing. On right side, bony lesion on distal humerus with proximal ulna with proximal R-U joint dislocation and associated distal radius-ulna lesions without any deformity.



**Fig.2** left distal femur, proximal tibia-fibula showing large bony lesions of osteochondroma. Associated small lesions are visible at distal tibia and proximal femur.



**Fig 3** MRI reports of right proximal humerus and left distal thigh stating multiple bony lesions at these locations.

### Discussion

Hereditary Multiple Exostoses (HME) is an autosomal dominant skeletal dysplasia which affects 0.9 to 2 individuals per 100,000<sup>2,4,6-8</sup>. It is a genetically heterogeneous disorder that has been associated with mutations in at least 3 different genes termed EXT genes. The three EXT loci have recently been mapped: EXT1 is in chromosomal regions 8q23-q24, EXT2 is on 11p11-p12, and EXT3 is on chromosome arm 19p. Epidemiologic analysis of linkage and mutation data indicate that mutations of EXT1 and EXT2 are likely to be responsible respectively for one half and one third of all cases of multiple hereditary exostoses whereas EXT3 which has not been fully isolated and characterized, is probably less frequently involved<sup>4,6</sup>. Although previously thought to have a male Predominance<sup>9</sup>, HME now appears to affect both sexes equally<sup>4</sup>. Exostoses are initially recognized and diagnosed in the first decade of life in over 80% of individuals with HME and are most commonly first discovered on the tibia or scapula as these are often the most conspicuous locations<sup>5</sup>. Penetrance of this condition is said to be 100% but expressivity is variable. Therefore in a family with a negative history, the patient may be the first person to demonstrate the clinical expression of the trait. It

is therefore not surprising that our one patient have a negative family history which may be due to this phenotypic variability or to the sporadic mutation reported in a number of patients with Hereditary Multiple Exostoses. The diagnosis of HME was made on the basis of clinical and radiological examinations. The clinical features of HME depends on the time of presentation, the site, the size and the extent of physal involvement in the pathology. Early presentation is characterized by painless bilateral multiple bony lumps at the ends of the long bones. Usually, the proximal humerus, distal radius and ulna, distal femur and proximal tibia are the favoured sites. Other sites of involvement include the apophyseal border of the scapula and pelvis<sup>5</sup>. When they present late pressure and obstructive symptoms, asymmetrical growth retardation and deformities may predominate. Thus pain, hyperaesthesia, limb-length discrepancy, wrist, ankle, forearm and leg deformities may be the presenting clinical features.

The most common deformities seen in HME include short stature, limb-length discrepancies, valgus deformities of the knee and ankle, asymmetry of the pectoral and pelvic girdles, lateral bowing of the radius with ulnar deviation of the wrist, and subluxation of the radial head<sup>4,5</sup>.

A few reported cases of urinary tract obstruction and spinal cord compression complicating multiple exostoses have been reported in the literature<sup>5</sup>.our case presented with bilateral symmetrical bony lumps in proximal humerus, the radius and ulna, femur, tibia and fibula, In addition the patient also presented with a limb length discrepancy of 2cm located in the left distal femur. The anatomic proximity of the lesion to the physis is responsible for its tethering effect on one side of the physis, thus producing an asymmetrical growth of the bone. This latter effect is the basis of the limb-length discrepancy and the observed forearm varus, ulnar deviation, genu and ankle valgum in HME. The thinner of the two bones in the forearm and the leg is usually more affected and this serves as the basis for the deformities in HME. Exostoses of the upper extremities frequently cause forearm deformities. The prevalence of such deformities has been reported to be as high as 40-60%<sup>4,5</sup>. Disproportionate ulnar shortening with relative radial overgrowth has been frequently described and may result in radial bowing<sup>5</sup>. Subluxation or dislocation of the radial head is a well-described sequelae in the context of these deformities and was seen in 8 of 37 elbows examined by Shapiro et al<sup>10</sup>.

Dislocation of radial head has been associated with a loss of pronation, greater ulnar variance, and functional impairment .The persistent pain and the increase in size of the proximal humeral exostosis in the 14-year old patient which were due to bursitis under the long head of biceps and pressure symptoms on adjacent nerves were eliminated immediately after excision of the exostosis. Both neurological and vascular problems can arise throughout the extremities as complications of HME. Ulnar neuropathy secondary to compression by an exostosis of the elbow has also been described.

Malignant transformation of a benign osteochondroma to a chondrosarcoma or other sarcoma is another complication of HME. Fortunately, most chondrosarcomas in this setting are low grade and can be treated with wide

excision. Patients with such lesions usually present with a painful mass. Rarely, nerve compression can be the presenting complaint. The reported incidence of malignant degeneration is highly variable, ranging from 0.5-25%<sup>8</sup>. The treatment of non-complicated cases of HME is masterly inactivity as it is inadvisable to operate before skeletal maturity for fear of damage to the physis. However, surgical excision is indicated only when the lesion causes pain, deformity, disability and when in close relationship with a neurovascular bundle. The aim of surgery is complete excision of the cartilaginous cap. Recurrence rate of about 2% is associated with incomplete excision. The management of secondary deformities depends on the severity and the age at presentation and may entail corrective osteotomy, timely epiphyseodesis and limb lengthening. One of our patients had excision of exostosis to relieve pressure symptoms.

### Conclusion

Thus, we have been able to use our patient to illustrate the clinical and radiological features. The pathogenesis of most of the pathologies in HME has been highlighted while the differential diagnosis and surgical options were mentioned.

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